STATEMENT OF RICHARD A. DENISON, Ph.D.
SENIOR SCIENTIST
ENVIRONMENTAL DEFENSE
www.environmentaldefense.org/go/nano

BEFORE
THE U.S HOUSE OF REPRESENTATIVES COMMITTEE ON SCIENCE

CONCERNING

ENVIRONMENTAL AND SAFETY IMPACTS OF NANOTECHNOLOGY: WHAT RESEARCH IS NEEDED?

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1875 Connecticut Avenue, NW · Washington, DC 20009 · Tel 202 387 3500 · Fax 202 234 6049 · www.environmentaldefense.org
New York, NY · Oakland, CA · Boulder, CO · Raleigh, NC · Austin, TX Project Offices : Boston, MA · Los Angeles, CA

Summary of Responses to the Committee's Questions

Question 1: Are current federal and private research efforts adequate to address concerns about environmental and safety impacts of nanotechnology? If not, what additional steps are necessary?

- Strong consensus that federal funding for risk research should be substantially increased
  At least $100 million annually for at least the next several years is needed
- Needed additional steps:
  NSET or a federal research agency should develop, direct an overall federal research strategy
  Draw on expertise of National Academies' Board on Environmental Studies and Toxicology
- Industry should fund research and testing on its products

Question 2: What are the primary concerns about the environmental and safety impacts of nanotechnology based on the current understanding of nanotechnology?

- Need for a lifecycle view, especially for dispersive applications of nanomaterials
- Novel properties of nanomaterials that may pose potential risks
  Potential to cross cell membranes
  Translocation of inhaled nanoparticles from lung to brain or into systemic circulation
- Lack of data on chronic toxicity, surprising results in short-term studies
  Carbon nanotubes (CNTs)
  C60 fullerenes (commonly known as buckyballs)
  Quantum dots
- Importance of surface area and surface properties
  Stability of coatings

Question 3: What should be the priority areas of research on environmental and safety impacts of nanotechnology? Who should fund and who should conduct that research?

- Fundamental need for government to develop or revise tools and methods to:
  Characterize, detect, measure and monitor for nanomaterials
  Assess biological and environmental fate and behavior
  Assess acute and chronic toxicity and ecotoxicity
- Government-led research to create database on representative, model nanomaterials
  Industries using these materials should also help fund this basic work
- Companies should have responsibility for testing products prior to commercialization

Question 4: What impacts are environmental and safety concerns having on the development and commercialization of nanotechnology-related products and what impact might these concerns have in the future?

- Real potential for public backlash if government does not identify, address risks up front
  As with GMOs, could delay or even prevent realization of potential benefits
  Public identifies up-front safety testing, more information as critical to building trust
- Extent of safety assessment conducted could become a competitive issue for US industry
  Companies indicate they want science-based regulation to provide a more level playing field
- Public and private interests are best served by identifying potential risks now when they can be avoided, rather than paying later to remediate resulting harms

I. Introduction[1]

A remarkable and unusual consensus has emerged with respect to the federal government's role in nanotechnology: Organizations as diverse as environmental NGOs, large chemical companies, nanotech startups, insurance companies and investment firms all agree that the Federal Government should be immediately directing many more of the dollars it is currently investing in nanotechnology development toward identifying and assessing the potential risks of nanomaterials to human health and the environment. This Federal investment in risk research is essential to developing the basic infrastructure that will enable the private sector to fulfill its responsibility to identify, assess and reduce the potential risks associated with the nanomaterial-containing products before they are brought to market.

Nanotechnology, the design and manipulation of materials at the atomic scale, may well revolutionize many of the ways our society manufactures products, produces energy, and treats diseases. Hundreds of large and small nanotechnology companies are developing a wide variety of materials for use in electronics, medical diagnostic tools and therapies, construction materials, personal care products, paints and coatings, environmental cleanup, energy production and conservation, environmental sensors, and many other important applications.

Deliberate exploitation of properties that only become evident at the nanoscale is central to these applications. Such properties include highly specific binding over a huge surface that arises from tiny particle size, absorption and radiation of specific wavelengths of light, penetration of cellular barriers, and high tensile strength and durability. Carefully controlled, these properties may provide highly beneficial products. But these new and enhanced properties also raise the possibility of unintended adverse consequences for human health and the environment. The same binding properties that allow use of nanoparticles to deliver therapeutics to cancer cells may also, for example, deliver toxic substances to normal human cells, or to aquatic organisms if such materials are released or used in the ambient environment. The electrical properties that drive applications in computers can lead to oxidative damage in living tissues. It is essential that potential harms like these are identified and mitigated up front, prior to widespread commercialization and human and environmental exposure.

[1] A biography of Dr. Denison is attached. Several other Environmental Defense staff contributed to the preparation and content of this testimony: Dr. John Balbus, Health Program Director, Karen Florini, Senior Attorney, and Scott Walsh, Project Manager.

II. Responses to the Committee's Questions

This testimony provides Environmental Defense's responses to the four questions posed by the Committee in its invitation letter.

A. Committee question #1: *Are current federal and private research efforts adequate to address concerns about environmental and safety impacts of nanotechnology? If not, what additional steps are necessary?*

In our view, current federal and private research efforts are far from adequate to address concerns about environmental and safety impacts of nanotechnology, and funding for such efforts should be substantially increased.

The U.S. government, as the largest single investor in nanotechnology research and development, needs to spend much more to assess the health and environmental implications of nanotechnology and ensure that the critical research needed to identify potential risks is done expeditiously. Through the National Nanotechnology Initiative (NNI), the federal government spends roughly $1 billion annually on nanotechnology research and development. Of this, environmental and health implications research accounted for only $8.5 million (less than 1 percent) in FY 2004, and is expected to increase to only $38.5 million (less than 4 percent) in FY 2006.

In a rare example of convergence from sectors that often have highly divergent views, environmentalists, industry and the insurance and investment communities are all calling for dramatic increases in federal funding on the health and environmental implications of nanotechnology. For example, in June 2005 the CEO of DuPont and the President of Environmental Defense coauthored an opinion editorial in the Wall Street Journal calling for an increase in such funding to at least $100 million annually. That same month, the American Chemistry Council's Panel on Nanotechnology and Environmental Defense issued a Joint Statement of Principles[2] stating: "A significant increase in government investment in research on the health and environmental implications of nanotechnology is essential." And in a recent report[3] on nanotechnology, Innovest, a leading investment research and advisory firm, has said: "We strongly support calls by others in the investment community for increased government funding of toxicology research. The NNI's lack of priority for this issue represents a missed opportunity to minimize uncertainty."

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[2] Environmental Defense and American Chemistry Council Nanotechnology Panel, "Joint Statement of Principles," Submitted as Comments on EPA's Notice of a Public Meeting on Nanoscale Materials, 70 FR 24574 – Docket OPPT-2004-0122, 23 June 2005, available online at www.environmentaldefense.org/documents/4857_ACC-ED_nanotech.pdf.

[3] Innovest (2005). *Nanotechnology: Non-traditional Methods for Valuation of Nanotechnology Producers*. New York, NY. Page 56. Available online at www.innovestgroup.com/publications.htm (accessed Nov. 2, 2005).

Similarly, at a briefing held on March 22, 2005, to preview the findings of a report by the President's Council of Advisors on Science and Technology (PCAST) that reviewed the NNI, John H. Marburger III, Science Adviser to the President and chief of the White House Office of Science and Technology Policy, stated that the toxicity studies now underway are "a drop in the bucket compared to what needs to be done."[4]

Our and others' calls for the U.S. government to spend at least $100 million annually on hazard and exposure research for at least the next several years is buttressed by experts' assessments of the cost to conduct the needed research, as well as by testing costs associated with hazard characterization programs for conventional chemicals, and the research budgets for a roughly analogous risk characterization effort on risks of airborne particulate matter.[5] While this level of risk research spending will represent a significant increase over current levels, it is still less than 10% of the overall federal budget for nanotechnology development. Moreover, it is a modest investment compared to the benefits of risk avoidance and to the $1 trillion contribution that nanotechnology is projected to make to the world economy by 2015.

What additional steps are necessary? We recognize that at present the NNI's Nanoscale Science, Engineering and Technology Subcommittee (NSET) serves primarily as a facilitator and coordinator of nanotechnology-related activities among the various Federal departments and agencies. In our view, ensuring that sufficient and appropriate risk research is carried out by the Federal Government may well require vesting the NSET or one of the lead federal health or environmental research agencies with responsibilities that go beyond these current functions. Sufficient authority to oversee and direct federal risk-related research is essential to ensure first, that the right questions are asked and answered, and second, that identified risks are comprehensively assessed and do not fall through the cracks between statutes, departments and agencies.

We therefore offer two proposals for your consideration. The first is to vest NSET or one of the lead federal health or environmental research agencies with:

- the task of developing an overall federal research strategy for identifying and assessing potential risks of nanomaterials;
- the authority to shape and direct the overall federal risk research agenda across agencies to ensure all critical needs are being addressed, ideally with some budgetary authority; and
- the responsibility to ensure that individual agencies have sufficient dedicated staff and resources to conduct or commission the needed research in their areas, and sufficient authority to identify and assess potential risks.

Our second proposal is that Congress should call on the NNI and its member agencies to request assistance from the National Academies, in particular the Board on Environmental

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[4] R. Weiss, "Nanotech Is Booming Biggest in U.S., Report Says," *Washington Post*, March 28, 2005, p. A6, available online at www.washingtonpost.com/wp-dyn/articles/A5221-2005Mar27.html.

[5] A full explication of the basis for the $100 million annual figure, which I submitted earlier this year to the National Research Council's Committee to Review the NNI, is available online at www.environmentaldefense.org/documents/4446_EnvironmentalDefenseStatementNRCNanopanel25Mar05.pdf

Studies and Toxicology (BEST). BEST should be asked to review the NNI agencies' ongoing research and research plans, offer its guidance on appropriate risk screening and assessment approaches, and help guide the development and implementation of the federal research strategy we call for above, to help ensure the right research is done. BEST has played an analogous role in the formulation and execution of the U.S. Environmental Protection Agency's research strategy for assessing the risks of airborne particulate matter.[6]

Of course, the U.S. government should not be the sole, or even the principal, funder and conductor of nanomaterial risk research. Other governments are also spending heavily to promote nanotechnology research and development, and they too should allocate some portion of their spending to address nanotechnology risks. And although government risk research has a critical role to play in developing the basic knowledge and methods to characterize and assess the risks of nanomaterials, private industry should fund the majority of the research and testing on the products they are planning to bring to market. Clearly, all parties will benefit if governments and industry coordinate their research to avoid redundancy and optimize efficiency.

B. Committee question #2: *What are the primary concerns about the environmental and safety impacts of nanotechnology based on the current understanding of nanotechnology?*

The primary concerns about nanomaterials' health and safety impacts arise both from consideration of the inherent nature and novel properties of at least certain nanomaterials, and from surprising results seen in many of the relatively small number of nanotoxicity studies conducted to date. As described below, various nanomaterials have been demonstrated to have the potential to:

- cross physiological barriers (lung-blood and blood-brain) and enter the systemic circulatory system, thereby posing risks to organ systems removed from the site of entry;
- evade the body's usual metabolic and immune defense mechanisms;
- penetrate cell membranes;
- directly interact and possibly interfere with cellular components;
- deliver secondary molecules to intracellular targets, or reach non-target cells or organs; and
- persist and accumulate in the body or the environment.

Scientists are only beginning to examine the extent to which these behaviors can result in significant toxicological impacts, and if so, at what levels of exposure. Likewise, as yet there is little understanding of the mechanisms that lead to the biological effects that have been observed in toxicity studies. Such effects, further described below, include the potential to:

- kill skin cells in culture;

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[6] Board on Environmental Studies and Toxicology, *Research Priorities for Airborne Particulate Matter: I. Immediate Priorities and a Long-Range Research Portfolio*, Committee on Research Priorities for Airborne Particulate Matter, National Research Council, 1998; and *Research Priorities for Airborne Particulate Matter: IV. Continuing Research Progress*, 2004, both available online at: books.nap.edu/catalog/6131.html, and books.nap.edu/catalog/10957.html.

- damage brain tissue in mammals and in fish;
- impair lung function and generate unusual granulomas in the lungs of rodents; and
- kill microorganisms, including ones that may constitute the base of the food web.

Need for a lifecycle view, especially for dispersive applications of nanomaterials

Some uses of nanomaterials already on the market, and others now in the pipeline, will result in exposure of humans or the environment, either through direct application or dispersive use. Some of these exposures reflect the inherent nature of the product or application, such as in uses of nanomaterials in drugs and cosmetics, and in remediation of groundwater contamination. Other products may also entail substantial exposures, though not necessarily during a product's use. For example, tennis rackets, automobile running boards, and other products contain carbon nanotubes embedded within resins or other matrices. While exposure to individual nanoparticles during such a product's intended use seems unlikely, a lifecycle view is critical to understanding the potential risks. A product's lifecycle includes not just the product's use phase, but also its manufacture (and the manufacture of its components) and its disposal or recycling/reclamation. Human or environmental exposures during these other stages may be substantial. For instance, nanomaterials present in cosmetics and sunscreens will be washed off and enter water supplies – as has already been demonstrated for pharmaceuticals and ingredients in personal care products. And although computer users are highly unlikely to inhale carbon nanotubes bound in their computer screen, exposure potential may dramatically increase when recyclers ultimately grind up those screens for other uses. Human exposures are most obvious for the workers doing the grinding, but may also be associated with the various stages of the lifecycle of the subsequent product(s) – especially if knowledge of the presence of nanomaterials is not carried downstream along with the material itself.

Novel properties of nanomaterials that may pose potential risks

Potential to cross cell membranes: In some cases, the very properties that make nanomaterials uniquely useful in biomedical or other commercial applications also raise the potential for novel mechanisms and targets of toxicity. For example, the ability of certain nanoparticles to penetrate cell membranes, which new applications to deliver targeted therapies exploit, suggests that nanoparticles will also be able to cross physiologic barriers and enter body compartments that larger particles and smaller molecules do not readily access. Particles of different sizes gain entry into the body's cells via very different mechanisms. Those larger than 500 nanometers (nm) primarily gain entry through active endocytosis; those smaller than 200 nm gain entry through a variety of active and non-active mechanisms.[7] One study of 20-nm polystyrene beads suggests that they enter cells by passing directly through membranes – without requiring specific transport mechanisms. Once inside the cells, these nanoparticles distribute throughout the cytoplasm and appeared to bind to a variety of cell structures.[8]

[7] Rejman, J. et al. 2004. "Size-dependent internalization of particles via the pathways of clathrin- and caveolae-mediated endocytosis." *Biochem J.* 377: 159-69.

[8] Edetsberger, M., et al. 2005. "Detection of nanometer-sized particles in living cells using modern fluorescence fluctuation methods." *Biochem. Biophys. Res. Commun.* 332(1): 109-116.

The manner in which different individual and aggregated nanoparticles may interact with critical cell structures is poorly understood, and cannot be inferred from studies of chemical agents or randomly generated nanoparticles. Surface modifications may allow nanoparticles to bind to cell surface receptors and either avoid uptake[9] or be taken up by specific transport mechanisms, allowing cell targeting for therapeutic agents. It is clear that subtle variations in nanoparticle surfaces, whether due to intentional coating prior to entry into the body or unintentional surface binding or to coating degradation once inside the body, can have dramatic impacts on where and how nanoparticles gain entry into cells, as well as where and how they are transported within cells after entry. Understanding the implications of such transport, as well as ensuring the stability of surface properties throughout the lifespan of manufactured nanoparticles, will be critical to assuring safety.

Preliminary efforts to use nanoparticles for therapeutic interventions indicate that at least some nanomaterials have unanticipated toxic effects – effects that have been detected only because of the testing that routinely occurs in the course of drug development. In one example, researchers developing nanoparticles designed to target gliosarcoma tumor cells noted that, of twenty such materials, all caused adverse effects on the reticular endothelial system (comprised of the liver, spleen and peripheral lymph nodes) and the kidneys.[10]

Translocation of inhaled nanoparticles from lung to brain or into systemic circulation: Nanoparticles can deposit throughout the respiratory tract when inhaled. Some of the particles settle in the nasal passages, where they have been shown to be taken up by the olfactory nerves and carried past the blood-brain barrier directly into brain cells. Smaller nanoparticles have been shown not only to penetrate deeply into the lungs, but to readily cross through lung tissue and enter the systemic circulation. These and other studies suggest that some nanomaterials can evade the lung's normal clearance and defense mechanisms. This potential for rapid and widespread distribution within the body offers promise of a new array of diagnostic and therapeutic applications for these substances – but it also heightens the importance of having a full understanding of their toxicity.

<u>Lack of data on chronic toxicity, surprising results in short-term studies</u>

No studies on reproductive toxicity, immunotoxicity, or chronic health effects such as cancer or developmental toxicity of nanomaterials have yet been published.[11] Of the limited number of short-term studies completed to date, however, several have found a variety of adverse effects associated with each of the major classes of nanomaterials now being produced.

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[9] Gupta, A. et al. 2004. "Lactoferrin and ceruloplasmin derivatized superparamagnetic iron oxide nanoparticles for targeting cell surface receptors." *Biomaterials*. 25: 3029-40.

[10] Institute of Medicine of the National Academies. 2005. *Implications of nanotechnology for environmental health research*. The National Academic Press. Washington, D.C.

[11] Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies (2005). "Nanotechnology. Environmental and Health Implications. A database of current research." Available at www.nanotechproject.net.

Studies in which **carbon nanotubes (CNTs)** were instilled into the lungs of rodents have consistently demonstrated that CNTs cause unusual localized immune lesions (granulomas) within thirty days, and other signs of lung inflammation.[12,13,14] One of these studies[15] – which utilized lower doses corresponding to the equivalent dose that would be experienced after a few weeks exposure at the current OSHA workplace standard for respirable particles – also found that single-walled CNTs cause dose-dependent fibrosis even in areas of the lung far removed from the sites of particle deposition. One study of multi-walled CNTs showed similar lung toxicity, especially after the material was finely ground.[16] Oxidative stress may be part of the mechanism behind the damage to lung tissue that has been observed in these studies of carbon nanotubes. Single and multi-walled CNTs have also been shown to induce oxidative stress in skin cells.[17,18,19] These studies raise concern for potential toxicity at the beginning or end of the lifecycle of products containing CNTs, through workplace exposures or if CNT-containing products undergo weathering, erosion or grinding during recycling or disposal.

C_{60} fullerenes (commonly known as buckyballs) have been less well-studied in mammalian models. A recent study of buckyballs found that, although individual buckyballs do not dissolve well in water, they have a tendency to form aggregates that are both very water-soluble and bacteriocidal, a property that raises strong concerns of ecosystem impacts because bacteria constitute the bottom of the food chain in many ecosystems.[20] They are also capable of being transported via the gills from water to the brains of fish, where they can cause oxidative damage to brain cell membranes.[21] In experiments with human cultured cell lines, buckyballs show high toxicity, causing oxidative damage to cell membranes that leads to cell death.[22]

Quantum dots can be made of a variety of inherently toxic materials, including cadmium and lead. As some of the key applications of quantum dots include diagnostic imaging and medical therapeutics, quantum dots have been studied relatively extensively in biological systems, although only a small portion of this research has focused on potential toxicity. Studies

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[12] Lam, C. et al. 2003. "Pulmonary toxicity of single-wall carbon nanotubes in mice 7 and 90 days after intratracheal instillation." *Toxicol. Sci*. 77: 126-134.
[13] Warheit, D. et al. 2004. "Comparative pulmonary toxicity assessment of single-wall carbon nanotubes in rats." *Toxicol. Sci*. 77: 117-25.
[14] Shvedova, A. et al. 2005. "Unusual inflammatory and fibrogenic pulmonary responses to single-walled carbon nanotubes in mice." *Am. J. Physiol. Lung Cell. Mol. Physiol*. 289(5): L698-708.
[15] Shvedova et al. 2005, *op.cit.*
[16] Muller, J. et al. 2005. "Respiratory toxicity of multi-wall carbon nanotubes." *Toxicol. Appl. Pharmacol*. 207: 221-31.
[17] Monteiro-Riviere, N. et al. 2005. "Multi-walled carbon nanotube interactions with human epidermal keratinocytes." *Toxicol Lett*. 155: 377-384.
[18] Manna, S. et al. 2005. "Single-walled carbon nanotube induces oxidative stress and activates nuclear transcription factor- kb in human keratinocytes." *Nano Lett*. Vol. 5, 9: 1676-1684.
[19] Shvedova, A. et al. 2003. "Exposure to carbon nanotube material: assessment of nanotube cytotoxicity using human keratinocyte cells." *J. Toxicol. Environ. Health A*. 66:1909-1926.
[20] Fortner, J. et al. 2005. "C60 in water: nanocrystal formation and microbial response." *Environ. Sci. Technol*. 39: 4307-16.
[21] Oberdorster, E. 2004. "Manufactured nanomaterials (fullerenes, C60) induce oxidative stress in the brain of juvenile largemouth bass." *Environ. Health Perspect*. 112: 1058-62.
[22] Sayes, C. et al. 2004. "The differential cytotoxicity of water-soluble fullerenes." *Am. Chem. Soc*. 4: 1881-1887.

performed to date have mainly been *in vitro* cytotoxicity assays that measure cell damage or death. While results have been somewhat inconsistent, studies that used longer exposure times were more likely to demonstrate significant toxicity.[23] Quantum dots typically have a core made of inorganic elements, but they are generally coated with organic materials such as polyethylene glycol to enhance their biocompatibility or target them to specific organs or cells. Some coatings initially decrease toxicity by one or more orders of magnitude, but the coatings are known to degrade when exposed to air or ultraviolet light, after which toxicity increases. While the presumption has been that this cytotoxicity is caused by leakage of toxic heavy metals (e.g., cadmium or selenium) from the core, there is evidence that some of the molecules used as coatings may have independent toxicity.[24] Significant questions remain about the safety of quantum dots based on the available *in vitro* studies.

Although the doses and methods of administration used in many of these studies do not necessarily reflect mirror likely exposure scenarios, the results strongly suggest the potential for some nanomaterials to pose significant risks.

Importance of surface area and surface properties

Understanding the behavior of nanoparticles requires careful characterization of their surface properties. For a given mass of particles, surface area increases exponentially with decreasing diameter (and increasing number). This increased surface-area-to-volume ratio may be a critical feature in understanding the toxicity of nanomaterials. For example, it leads to higher particle surface energy, which may translate into higher reactivity.[25] In addition, the combination of high surface area and small size may give nanoparticles unusual catalytic reactivity due to quantum effects, such as those seen with gold nanoparticles.[26] This combination of enhanced surface area and enhanced surface activity lends far greater complexity to the characterization of nanoparticles, and also precludes easy extrapolation about potential toxicity.

Stability of coatings: Most research to date has used prototypical or "plain" nanoparticles, such as uncoated buckyballs and carbon nanotubes. The few studies that have looked at the effects of variations and coatings have shown that these changes modify (typically reduce) the toxicity of the original particle, further complicating the picture by raising the question of how these coatings may degrade over time within the body or in the environment.

In sum, the limited information available to date indicates that nanomaterials can both: a) exhibit novel properties and behavior that facilitate access to organisms, including specific cells or organs, raising the potential for biologically significant exposures to occur should such

[23] Hardman, R. 2005. "A toxicological review of quantum dots: toxicity depends on physico-chemical and environmental factors." *Environ. Health Persp*. Nat. Inst. of Environ. Health Sci. doi: 10.1289/ehp.8284. Available at: http://dx.doi.org. (Accessed on November 4, 2005).
[24] Hardman et al. 2004, *op. cit.*
[25] Oberdorster, G. et al. 2005. "Principles for characterizing the potential human health effects from exposure to nanomaterials: elements of a screening strategy." *Part. Fibre Toxicol.* 2: 8.
[26] Daniel, M. et al. 2004. "Gold nanoparticles: assembly, supramolecular chemistry, quantum-size-related properties, and applications toward biology, catalysis, and nanotechnology." *Chem. Rev*. 104: 293-346.

materials be released, and b) exhibit toxicity to a range of cell and organ types both *in vitro* and *in vivo*.

C. Committee question #3: *What should be the priority areas of research on environmental and safety impacts of nanotechnology? Who should fund and who should conduct that research?*

There is broad agreement among stakeholders that addressing the potential risks of nanotechnology will be an unusually complex task. Despite its name, nanotechnology is anything but *singular*; it is a potentially limitless collection of technologies and associated materials. The sheer diversity of potential materials and applications – which is a source of nanotechnology's enormous promise – also poses major challenges with respect to characterizing potential risks.

Even before the research that will allow hazards and exposures to be quantified, a number of more fundamental needs must be addressed. It is already clear that even extremely subtle manipulations of a nanomaterial can dramatically alter its properties and behavior: Tiny differences in the diameters of otherwise identical quantum dots can alter the wavelength of the light they fluoresce; slight changes in the degree of twist in a carbon nanotube can affect its electrical transmission properties. A priority must be to develop the means to sufficiently characterize nanomaterials and to systematically describe and detect such subtle structural variations – a clear prerequisite to being able to conduct and interpret the results of toxicological testing and exposure measurements. Emphasis needs to be placed, therefore, on developing methods, protocols and tools needed to *characterize* nanomaterials, and to *detect and measure* their presence in a variety of settings (e.g., workplace environment, human body, environmental media).

Among the types of risk research that are needed for specific nanomaterials are the following:

- Material characterization (in manufactured form(s), during use, in emissions, in wastes, in products; in environmental media, in organisms)
- Biological fate (extent and rate of absorption, distribution, metabolism, elimination in mammals and other organisms)
- Environmental fate and behavior (persistence, transport between and distribution among media, transformation, bioaccumulation potential)
- Acute and chronic toxicity (related to both human and ecological health)

For each of these areas, existing testing and assessment methods and protocols need to be re-examined to determine the extent to which they can be modified to account for nanomaterials' novel characteristics or need to be supplemented with new methods. Similar challenges will arise with respect to methods and technologies for sampling, analysis and monitoring, all of which will be needed to detect nanomaterials and their transformation products in living systems and in various environmental media.

Another essential task for government-funded research is helping to create an initial database of toxicity data on representative or model nanomaterials. Doing so will help guide additional research by the private sector on their own nanomaterials, and will also lay the groundwork for the ultimate development of so-called "structure-activity relationships" (SARs) for nanomaterials. SARs are now widely used to reduce the amount of traditional toxicological testing needed to characterize conventional chemicals, by allowing the toxicity of an unstudied chemical to be estimated, based on its degree of structural similarity to chemicals that have been studied. Use of SARs is beneficial for several reasons: it's faster, it's cheaper, and it can minimize the need for testing using laboratory animals. But existing SAR models cannot simply be applied to nanomaterials: Because the models are based on the properties of bulk forms of conventional chemical substances, and because nanomaterials' novel and enhanced properties result from characteristics (e.g., size, shape) in addition to their molecular structure, existing models have little applicability to nanomaterials. In other words, the defining character of nanotechnology – the emergence of *novel* properties and behavior that cannot be predicted from the properties and behavior of their bulk counterparts – effectively precludes our relying on existing knowledge about the toxicity of conventional chemicals to predict the toxicity of nanomaterials. Only once enough data exist to correlate a nanomaterial's properties – or the changes in such properties that occur in the body or the environment – with observed patterns of toxicity, will nanomaterial-specific SARs be possible.

In sum, government needs to play the lead role in developing the *enabling infrastructure* for identifying and assessing nanomaterials' potential risks, including by developing and standardizing methods for:

- physical-chemical characterization of nanomaterials;
- sampling and analysis;
- detection and monitoring: in workplaces, air/waterborne releases, humans and other organisms, environmental media;
- assessing environmental fate and behavior;
- assessing biological fate and behavior, including generating and making available radiolabeled or otherwise traceable samples of key types of nanomaterials, for government's own and others' use in such fate studies;
- testing for acute and chronic toxicity, including the development and validation of non-animal test methods where doing so is scientifically appropriate, in order to minimize animal testing; and
- hazard, exposure and risk assessment.

As noted above, given its major investment in nanomaterials development, it is also appropriate for government to identify and conduct a full characterization and testing of a variety of "model" nanomaterials, although industries already using these materials should also help fund this basic work. Government should also take the lead on coordinating the efforts of private and public sectors, and for international cooperation and coordination of risk research.

None of the above should be construed, however, as a substitute for companies taking responsibility for (and bearing the financial burden of) all of the testing needed to ensure the

safety of their products prior to commercialization. To ensure maximum value and bolster public confidence in such research, we believe government and industry should commit to make publicly available *all* results, not just "interesting" ones that may be publishable in scientific journals or are required by law to be reported.

D. Committee question #4: *What impacts are environmental and safety concerns having on the development and commercialization of nanotechnology-related products and what impact might these concerns have in the future?*

While industry representatives may be in a better position to fully address this question, let me discuss one type of impact – public backlash – that could readily arise, given the growing evidence of potential health and environmental risks posed by certain nanomaterials, and the government's to-date-inadequate effort to identify and address such risks. The "risks" at issue here, therefore, are not only those related to health and the environment, but also risks to the very success of this promising set of technologies. If the public is not convinced that nanomaterials are being developed in a way that identifies and minimizes negative consequences to human health and the environment, a backlash could develop that delays, reduces, or even prevents the realization of many of the potential benefits of nanotechnology. As demonstrated with genetically modified organisms just a few years ago, rapid commercialization combined with a failure to address risks early on can lead to product bans and closed markets, resulting in this case in hundreds of millions of dollars in annual export losses for U.S. farmers and companies.

While little research into public attitudes toward nanotechnology has been conducted to date, some recently reported findings[27] are telling. In the context of finding generally low public awareness of nanotechnology and, among those with some awareness, a generally positive attitude, there were also some warning signs:

- Public trust in government appears to be low, with no more than half of the surveyed members of the public expressing confidence in Congress' or the Executive Branch's willingness or ability to manage nanotechnology-related risks.
- Suspicions of industry abound, with only a small percentage indicating that industry could be trusted to "self-regulate" and a concern that industry often rushes products to market without adequate testing.

Equally interesting were the responses concerning how the government and industry might best build public trust. For example:

- The two best ways identified by respondents to build public trust were requiring increased safety testing prior to introduction of products onto the market, and provision of more information to inform consumers' choices. Better tracking of risks for materials already on the market also ranked high.

[27] Woodrow Wilson International Center for Scholars, "Informed Public Perceptions of Nanotechnology and Trust in Government," authored by Dr. Jane Macoubrie, Washington, DC, September 2005, available online at www.wilsoncenter.org/news/docs/macoubriereport1.pdf.

- The lack of information on long-term health and environmental effects of nanotechnology and its products was frequently cited as a major concern.

Of course, all of these findings stress the need for more and better research into potential short- and long-term risks to be conducted now, prior to widespread commercialization of nanomaterial-containing products.

Finally, there is growing reason to expect that the extent of safety assessment conducted prior to market introduction of nanomaterial-containing products could well become a competitive issue. The investment firm Innovest notes in its recent report:

> "Off the record conversations with regulators indicate that Europe, the UK, and China are expecting to have some sort of binding requirement for companies within the next 2 to 4 years. China clearly states that its standards were designed to create a robust foundation for nanotechnology development in that region and that they expect their standards to impact the competitive landscape for nanotechnology."[28]

Clearly, the U.S. nanotechnology industry will benefit from an environment in which it can offer reassurances that the safety of its products has been assessed using robust methods and evaluation procedures. Industry itself recognizes as much; as the Innovest report goes on to note:

> "A significant portion of the more than 60 companies we interviewed indicated an interest in having some sort of standards in place. In many cases, they felt that science-based regulation would provide a more level playing field. The lack of adequate funding for toxicology research is, again, an issue here. ... Counter to intuition, our research shows that robust, science-based regulation can contribute to healthy market development."

III. Conclusion

In our view, both the public and private sectors' best interests are served by an investment to identify and manage potential nanotechnology risks now, rather than to pay later to remediate resulting harms. History demonstrates that embracing a technology without a careful assessment and control of its risks can be extremely costly from both human and financial perspectives. The failure to sufficiently consider the adverse effects of using lead in paint, plumbing, and gasoline has resulted in widespread health problems that continue to this day, not to mention extremely high remediation costs. Asbestos is another example where enormous sums of money were spent by private companies for remediation, litigation, and compensation, even beyond that spent by the public sector to alleviate harm to human health and the environment. Standard & Poor's has estimated that the total cost of liability for asbestos-related losses could reach $200 billion.[29]

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[28] Innovest (2005), *op. cit.*

[29] Standard & Poor's, *Insurance: Property-Casualty Industry Survey*, July 15, 2004.

The rapid commercialization of nanotechnology, coupled with the potential risks from at least certain nanomaterials as demonstrated in initial studies, lends urgency to the call for greater investment in risk research from the outset. Government and industry have done a great job so far in accentuating nanotechnology's potential upsides and in accelerating its development, but they have yet to come to terms with their equally critical roles in identifying and avoiding the downsides. A far better balance between these two roles must be struck if nanotechnology is to deliver on its promise without delivering unintended adverse consequences.

Fortunately, nanotechnology development and commercialization is still at an early stage, so it is not too late to begin managing this process wisely. Given the length of time it will take to develop an adequate understanding of the potential risks posed by such a wide variety of nanomaterials, and to apply this knowledge to inform appropriate regulation, it is imperative to take action now.

Nanotechnology offers an important opportunity to apply the lessons from prior mistakes by identifying risks up front, taking the necessary steps to address them, and meaningfully engaging stakeholders to help shape this technology's trajectory. In short, there is an opportunity to get nanotechnology right the first time.

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Attachment

Biography of Richard A. Denison, Ph.D.

Dr. Denison is a Senior Scientist in Environmental Defense's Environmental Health Program, working in its Washington, D.C. office. He specializes in hazard and risk assessment and management for industrial chemicals (including nanomaterials), and associated policy and regulatory issues. Dr. Denison is a member of USEPA's Pollution Prevention and Toxics Advisory Committee (NPPTAC), including its Workgroup on Nanotechnology, and serves on the Steering Group for Nanotechnology of the Organization for Economic Cooperation and Development (OECD).

Dr. Denison manages Environmental Defense's participation in the U.S. High Production Volume (HPV) Chemical Challenge Program, initiated by Environmental Defense, EPA and the American Chemistry Council to provide basic hazard data on the 2,200 chemicals produced in the U.S. in the largest quantities. He also represents Environmental Defense in proceedings of the Chemicals Committee and the Existing Chemicals Task Force of the OECD. He has authored several papers and reports, and is active in a variety of activities and fora, pertaining to nanomaterials and chemicals regulation and policy at the federal and state levels and internationally.

Dr. Denison earned a Ph.D. in Molecular Biophysics and Biochemistry from Yale University in 1982. He joined Environmental Defense in 1987, after several years as an analyst and assistant project director in the Oceans and Environment Program, Office of Technology Assessment, United States Congress.